UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/003,869	01/07/1998	NIGEL ROBERT ARNOLD BEELEY	231/181	9574

7590 05/07/2002

BBROBECK, PHLEGER & HARRISON, LLP.
12390 EL CAMINO REAL
SAN DIEGO, CA 92130-2081

EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1653	21

DATE MAILED: 05/07/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/003,869	BEELEY ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 January 2002 and 11 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30 and 32-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 January 1998* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13,19* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The Examiner in charge of this application has been changed. However, the Group and/or Art Unit location of your application in the PTO remains the same. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1653.

2. The request filed on 1/24/02 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/003,869 is acceptable and a CPA has been established. An action on the CPA follows.

ACKNOWLEDGMENT OF AMENDMENT, REMARKS, IDS AND STATUS OF THE CLAIMS

3. The amendment and remarks filed 1/24/02 and information disclosure statement (IDS) and Form PTO-1449 filed 8/6/01 and 2/11/02, respectively are acknowledged, entered and considered. In view of Applicant's request claims 16-22 and 32-34 have been amended. Thus, claims 1-30 and 32-34 are now pending in the application. In the previous Office action, claims 1-15 and 23-30 were allowed and claims 16-22 and 23-34 were objected. However, the objection, in view of Applicant's amendment filed 1/24/02 and the allowance, in view of the following rejection are withdrawn.

CLAIMS REJECTION-35 U.S.C. 112 1st PARAGRAPH.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-30 and 32-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for exendin or an exendin agonist compositions, and a method of reducing food intake in rodents (mice and rats) by administering an exendin or an exendin agonist formulation thereof, does not reasonably provide enablement for treating conditions or disorders which can be alleviated by reducing food intake in a subject including a human by administering a therapeutically effective amount of exendin or exendin agonist alone or in combination of leptin, amylin agonist, CCK and agonists according to Formulae I-III, wherein said condition or disorder is obesity, or Type II diabetes, or eating disorder, or insulin-resistance syndrome, and the method is intended to be useful for lowering the plasma glucose level, lowering the plasma lipid level, reducing the cardiac risk, reducing the appetite, and reducing the weight of a subject, and to a pharmaceutical formulations for use in the methods thereof as recited in claims 1-30 and 31-34. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant specification in Examples 1-4 show the injection of exendin in rodents (mice and rats) which resulted in reduction of food intake in normal and obese rodents. Examples 5-35

disclose the preparations of SEQ ID NOS:9-39, respectively, and Example 36 teaches the preparation of C-terminal carboxylic acid peptides corresponding to the sequences disclosed in Examples 5-35. Examples 37 describes the preparation of SEQ ID NO:7, and Examples 38-97 describe the preparation of SEQ ID NOS:40-99. Example 98 teaches the preparation of C-terminal carboxylic acid peptides corresponding to SEQ ID NOS:7, 40-61, 68-75, 78-80 and 87-96, and Example 99 teaches the preparation of C-terminal carboxylic acid peptides corresponding to SEQ ID NOS:62-67, 76, 77 and 81-86. Examples 100-188 describe the preparation of SEQ ID NOS:100-188, respectively. Example 189 teaches the preparation of C-terminal carboxylic acid peptides corresponding to SEQ ID NOS:100-166, 172-177, 179-180 and 185-188, and Example 190 teaches the preparation of C-terminal carboxylic acid peptides corresponding to SEQ ID NOS:167-171, 178 and 181-184. Thus, the instant specification discloses the preparations of various exendin or exendin agonist peptides and how to sequence them with protocols of how to administer the exendin or exendin agonist peptides including the level of the dosages. However, the scope of the instantly claimed invention are very broad and speculative in that there is/are no working example(s) or data or evidence which shows that the claimed exendin or exendin agonist and its biologically active analogue thereof individually or in combination with other compounds or compositions that affect satiety and are useful as a pharmaceutical composition by administering as an active ingredient in a therapeutically effective amount to effect the metabolic intervention to treat conditions or disorders which can be alleviated by reducing food intake in the manner claimed.

There is no evidence in the instant specification to use or administer the pharmaceutical formulation in therapeutically effective composition as claimed, except for the level of dosages, protocols and recitation of various references and incorporating improperly the references to show the effect of exendin or exendin antagonist for the reduction of food intake as disclosed on pages 1-14 and 33-39 in the instant specification. Further, Applicant acknowledges on page 5, lines 19 to page 6, lines 4, and as taught by Turton et al. (Nature, Vol. 379, pp. 69-72, 1996) that exendin (9-39) has been used to investigate the physiological relevance of central GLP-1 in control of food intake. GLP-1 administered by intracerebroventricular (ICV) injection inhibits food intake rats. This satiety-inducing effect of GLP-1 delivered ICV is reported to be inhibited by ICV injection of exendin. Thus, such statements discourage the use of GLP-1 and/or exendin as a composition (pharmaceutical agent) for reducing body weight, because central route of administration, such as the ICV route, are not feasible for treating obesity in humans. Therefore, in view of this acknowledgment, there are no sufficient data or evidence to substantiate such protocols of using a therapeutically effective pharmaceutical composition for treating conditions or disorders which can be alleviated by reducing food intake by administering an effective amount of an exendin or an exendin agonist alone or in combination with other compounds or compositions that affect satiety in the manner claimed. Hence, the only support for the claimed therapeutically effective pharmaceutical composition and method for treating conditions or disorders, including obesity, Type II diabetes, eating disorders, and insulin resistance syndrome, as well as lowering plasma glucose level, lowering the plasma lipid level, reducing the cardiac

risk, reducing the appetite, and reducing the weight of a subject including humans by administering a therapeutically effective dose of the pharmaceutical composition thereof in the specification is Applicant's supposition of the invention as recited in the protocols. Furthermore, Applicant's claims are directed to a very large number of compounds (i.e., exendin or exendin agonist and in combination with other compounds or compositions that affect satiety) by using specific therapeutically effective amount of pharmaceutical composition, and there are no objective factual evidence in the specification showing that treatment and/or amelioration has occurred using the specific therapeutically effective amount of pharmaceutical composition claimed. Thus, it is the Examiner's position that one can not administer specific effective amount of a pharmaceutical composition in all situations without appropriate testing which would require the exercise of undue experimentation, as for example, treating conditions or disorders which can be alleviated by reducing food intake to a subject including a human.

Therefore, in view of the above, it would include those that have not been shown or taught to be useful or enabled by the disclosed method of making and using the invention. Moreover, undue experimentation is necessary to determine if and under what conditions, the claimed invention as broadly claimed is enabled, since a vast range of pharmaceutical composition in all kinds of possible compounds are contemplated and are encompassed as well as wide range of situations. The results desired appear to be highly dependent on all variables, the relationship of which are not present in the specification. Hence, one of ordinary skill in the art would not be able to identify all the pharmaceutical preparations with the various exendin or

exendin agonists thereof either alone or in combination with other compounds or compositions that affect satiety having all kinds of concentrations intended to be effective for the claimed purpose as encompassed in the claims would be effective and under what conditions.

Further, the first paragraph of 35 U.S.C. 112 requires, inter alia, that a patent specification provide sufficient guidance to enable a person skilled in the art to make and use the claimed invention without undue experimentation. In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991). While patent Applicants are not directed to disclose every species that falls within a generic claim, id. At 496, 20 USPQ2d at 1445, it is well settled that "the scope of the claims must bear a reasonable correlation to the scope of the enablement provided by the specification". In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Where practice of the full scope of the claims would require experimentation; factors to be considered in determining whether a disclosure would require undue experimentation ..... include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. In re Wands, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Therefore, applying the Wands factors to the facts of this case, one of skill in the art would find that undue amount of experimentation would be required to practice the full scope of the extremely broad claims fro the reasons given above. Thus, in view of the quantity of

experimentation necessary, the lack of adequate guidance or working examples or data and the breadth of the claims; the claims are not commensurate in scope with the enabling disclosure. Accordingly, filing of evidence commensurate with the scope of the claims or amendment of the claims to what is supported by the enabling disclosure is suggested.

CLAIMS REJECTION-35 U.S.C. § 112 2nd PARAGRAPH

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5-6, 16-22, 24-27 and 32-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of

the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 5 recites the broad recitation about 10 µg to about 5 mg, and the claim also recites about 30 µg to about 5 mg which is the narrower statement of the range/limitation.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 6 recites the broad recitation about 10 µg to about 2 mg, and the claim also recites about 30 µg to about 2 mg which is the narrower statement of the range/limitation.

Claims 19 and 32-34 are indefinite in the recitation the acronym "CCK". Use of the full terminology at least in the first occurrence would obviate this rejection.

Claims 20-22 and 32-34 are indefinite and confusing in referring back to Formulae I, II, III, respectively in the specification because referring back to a Formula or a Figure or a Table is not acceptable claim language. Such material should be incorporated within the claim language. Further, it is long standing Office practice that claims should be complete and self-contained and incorporation into claims by express reference to the specification is not permitted and should not be relied on to define the invention (Ex parte Fressola, Bd. Pat. Appl. & Inter., 5/11/93, p.1608).

CLAIM REJECTION-35 U.S.C. § 102(b)

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 23-30 and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Eng (U.S. Patent No. 5,424,286).

Eng discloses a pharmaceutical composition comprising exendin-3 or exendin-4, fragments thereof, or any combination thereof for treatment of diabetes mellitus and the prevention of hyperglycemia (See e.g., Abstract and Summary of the Invention). Thus, the reference clearly discloses a composition comprising an effective amount of an exendin or an exendin agonist, alone or in combination with other compounds or compositions that affect satiety as claimed in claims 23-30 and 34. However, the reference does not disclose the intended

use of exendin or exendin antagonist for "treating conditions or disorders which can be alleviated by reducing food intake, wherein the conditions or disorders includes obesity, eating disorders, insulin resistance syndrome, lowering the plasma lipid level, reducing the cardiac risk, reducing the appetite, and reducing the weight of the subject". Although, the reference teaches the use of exendin or exendin antagonist for "treatment of diabetes and lowering the plasma glucose level", nevertheless, a statement of usefulness or contemplated use of a claimed compound or composition in a claim is usually given little weight in distinguishing over the prior art. In re Maeder et al. (CCPA 1964) 337 F2d 875, 143 USPQ 248; In re Riden et al. (CCPA 1963) 318 F2d 761, 138 USPQ 112; In re Sinex (CCPA 1962) 309 F2d 488, 135 USPQ 302. Thus, in the absence of evidence to the contrary or specific structural limitations, the claimed composition of an exendin or an exendin antagonist disclosed by the reference anticipates claim 23-30 and 34 as drafted.

CLAIMS REJECTION-35 U.S.C. §103(a)

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) a patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-30 and 32-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goldstone et al. (FEBS Letters, Vol. 415, pp. 134-138, 1997) in view of Eng (U.S. Patent No. 5,424,286).

Goldstone et a. teach the interaction of leptin with GLP-1 to reduce food intake and body weight in rodents. Based on this interaction, the reference also, investigated the effects of CNS GLP-1 receptor blockade, using ICV exendin (9-39), on the anorectic and weight reducing actions (See e.g., abstract). On page 137, the reference concludes by stating that the administration of leptin, GLP-1 and exendin (9-39) support for a potential role in the control of feeding and body weight. Thus, the reference clearly shows that use of exendin in combination with compounds such as leptin and GLP-1 that affect satiety reduced food intake and body weight in rodents.

The reference of Goldstone et al. differs from claims 1-30 and 32-34 in failing to teach the use of various exendin and exendin antagonists for treating conditions or disorders which include obesity, diabetes, eating disorders, insulin resistance syndrome, lowering the plasma glucose level, lowering the plasma lipid level, reducing the cardiac risk, and reducing the appetite of the subject". However, the secondary reference of Eng teaches as discussed above under the rejection of 102(b) a pharmaceutical composition comprising exendin-3 or exendin-4, fragments thereof, or any combination thereof for treatment of diabetes mellitus and the prevention of hyperglycemia. Thus, the reference clearly discloses a composition comprising an effective amount of an exendin or an exendin agonist, alone or in combination with other compounds or compositions that affect satiety by treating diabetes and lowering the plasma glucose level.

Thus, the secondary reference clearly teach the use of exendin or exendin antagonist for treatment of diabetes and prevention of hyperglycemia (i.e, lowering the plasma glucose level). Although, the secondary reference does not teach a method for reducing food intake and body weight in a subject; however, such metabolic intervention intended to an effective treatment to reduce food intake and body weight is taught by the primary reference. Therefore, given the teachings of the secondary reference, one of ordinary skill in the art would have been motivated to adapt the above scheme of using exendin or exendin antagonist alone or in combination with other compounds or composition that affect satiety, because such features are known in the art. Hence, including such features into the composition of the primary reference in view of

secondary reference, would have obvious to one having ordinary skill in the art to obtain the known and recognized functions and advantage thereof.

With respect to the amount of dosages, although, the prior art does not teach the dosages in the manner claimed; however, it would be conventional and within the ordinary skill in the art to which this invention pertains to select the appropriate optimum dosage of specific exendin or exendin antagonist peptide for the intended purpose of formulating a therapeutically effective pharmaceutical composition. Thus, in view of this, the subject composition may be used in combination with other materials to provide a wide variety of applications or may be tailored for specific applications, absence of sufficient objective factual evidence or unexpected results to the contrary.

CONCLUSION AND FUTURE CORRESPONDENCE

8. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (703) 308-3966. The examiner can normally be reached on Monday through Friday from 5:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (703) 308-2923. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Christopher S. F. Low

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Mohamed/AAM

May 6, 2002